Comparing the clinical effectiveness of two cryotherapy techniques for the treatment of plantar warts

Comparación de la eficacia de dos técnicas de crioterapia para el tratamiento de las verrugas plantares

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ABSTRACT
Objective. To compare two techniques of Cryotherapy for clinical effectiveness, pain, and effect on the quality of life of patients when treating plantar warts.
Method. A quasi-experimental matched subject study was conducted. Twenty subjects with a newly diagnosed plantar wart were recruited. Subjects were matched for confounding variables in relation to site of lesion, gender and age, and were divided into two groups. Group A (n=10) were treated using the CO_2 Gun & Probe technique whilst Group B (n=10) were treated using the Portable N_2O pressurized spray technique. The plantar warts were measured at time 0 (before treatment) and Time 1(3 weeks following treatment) using a metre ruler. The Foot Function Index and the Visual Analog Scale for pain assessment during treatment were also used.
Results. The study found no significant difference in the effectiveness (p= 0.387), pain caused during treatment (P=0.855) and FFI scores (p=0.172) for total change in QOL in the study group when comparing both treatments. However, comparison of the mean scores showed that the CO_2 Gun & Probe method was slightly more effective in reduction of size. Pain during treatment was almost identical when using both techniques. The FFI scores on all 3 subscales (Pain, Disability and Activity Limitation) showed a larger increase in the CO_2 Gun & probe method, when compared to the pressurized N_2O Portable device.
Conclusions. Although this study has found no significant difference between two different techniques of cryotherapy, mean differences have indicated that the CO_2 Gun & Probe technique is more effective in reducing the size of the warts when compared to the N_2O Pressurized Spray Technique; however the CO_2 Gun & Probe technique caused a larger impact on quality of life. Recommendations from this study suggest that careful consideration is required when selecting a treatment for plantar warts and furthermore patients should be advised on the likely outcomes of each treatment before any intervention.
Keywords: plantar warts; cryotherapy; nitrous oxide; carbon dioxide; quality of life.

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1. INTRODUCTION

Plantar warts are one of the most common dermatological infections overall[1]. Despite years of medical research and literature on the subject area, high quality evidence on the effectiveness of most treatments for removal of warts is lacking and no treatment has yet been proven to be 100% effective[2]. For this reason, many NHS Trusts view plantar warts as a very low priority as far as providing treatments[3]. However plantar warts are not only known to cause pain, they can be a detriment to a patient's quality of life due to embarrassment, fear of discrimination and frustration due to recurrence and persistence of the wart[4]. The high incidence of this condition and the associated complaints have inspired many authors to explore the available treatments for the fastest eradication of warts to relieve the patients from pain and allowing them to continue with their regular lifestyle[5]. Available treatments for plantar warts vary from simple topical application of salicylic acid, to intralesional injection of antivirals[2].

Warts can be cleared using cryotherapy either by stimulation of a local inflammation that triggers a cell mediated response or else by necrotic destruction of the viral keratinocytes[6]. The Gun & Probe type using Carbon Dioxide (CO_2) involves a metal probe which makes direct contact with the skin. A layer of KY Jelly is applied to the probe which is the pressed firmly against the lesion. The freezing continues for about 2-3 minutes or until a 1-3 mm halo appears around the lesion. This technique works by intentionally damaging the surrounding tissue, triggering an inflammatory reaction which forms a blister that helps to expel the viral mass. Another commonly adopted technique is that of using a portable Nitrous Oxide (N_2O) cryotherapy device. This works using small pressurized cartridges which are replaced on every use. This allows easy transportation. However the method of achieving results differs from the other technique mentioned above. This technique, according to the manufacturer documentation[7], attempts to clear the wart by means of necrotic destruction of the viral mass, specifically avoiding damage to the healthy tissue. The N_2O is sprayed directly onto the lesion and usually involves a circulatory or zig-zag motion while spraying. The device penetrates at a rate of 1mm per 5 seconds to a maximum of 3mm. The duration of treatment varies according to the size of the lesion however treatment time generally does not exceed 60 seconds. The treatment is followed by a second freeze 30 seconds after the first.

The purpose of this study is to compare two Techniques of Cryotherapy, The CO_2 Gun & Probe technique and the Portable N_2O pressurized spray technique for clinical effectiveness, pain, and effect on the quality of life of the patient when treating plantar warts after a single application. The two techniques being presently evaluated in this study have never been compared before internationally for clinical effectiveness although they are both known to be used. No published papers documenting their success rates or otherwise are available[3]. Results of this study aim to provide health care professionals with key information on which of the two techniques is the most clinical effective for removal of plantar warts.

2. METHOD

This study includes a clinical trial using a quasi-experimental matched subject design and was carried out at Birkirkara Primary Health Centre, Malta between October 2011 and February 2012. This study examined a convenient sample of 20 patients suffering from one or multiple plantar warts which had not received prior treatment. This study was approved by the University Research Ethics Committee and all participants provided informed consent before any data collection. All investigations were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2000[8]. Participants were eligible for the study if they were aged 18 years or over and had a plantar wart that, in the opinion of a healthcare professional, was suitable for treatment with both cryogens used in this study (carbon dioxide versus nitrous oxide). Participants were excluded from the study if they had impaired healing such as diabetes or peripheral vascular disease, were immunosuppressed or were taking immunosuppressant drugs such as oral corticosteroids, had neuropathy, were receiving renal dialysis, had

cold intolerence such as Raynaud's syndrome or had conditions such as cryoglobulinaemia, cryofibrinogenaemia, collagen or autoimmune disease. The examination and treatment methods were carried out by the same investigator to ensure uniformity.

For the purpose of this study 20 subjects were recruited and assigned into two groups, A and B. Ten informed consenting participants in group A received treatment via the CO_2 Gun & Probe Method whilst another ten informed consenting participants in group B received treatment via the portable N_2O Pressurized Spray method.

Various tools were used in this study for data collection. These included the Foot Function Index (FFI)[9], the Visual Analog Scale (VAS) and a sterile meter ruler. Further to these tools a demographic data collection sheet was devised to gather all the necessary data required such as age, gender and size and location of wart. Subjects were interviewed twice during the study, at Time 0 and at Time 1 (3 weeks after their 1st visit). Subjects were asked to fill in the Foot Function Index (FFI). This questionnaire gave the researcher insight on how the patient was living with the current foot condition, and how the wart was affecting the quality of life of the subject. The diameter of the lesion was measured, after debridement, using a meter ruler – a graded sterile scalpel handle with a millimetre scale. This reading was checked by a second podiatrist for tester reliability. A total of 3 reading were taken every time, and the mean reading was recorded on the demographic sheet.

The participants were divided into two groups and matched for age, gender and location of wart, using convenience sampling. The first patient recruited was assigned to Group A. When a suitable match was found, the matching patient was assigned to Group B. This was repeated until a total of 20 participants were recruited.

3. INTERVENTION

Group A received the following treatment: Cryotherapy using Carbon Dioxide as a Cryogen using the Gun & Probe technique. This involved a metal probe which came into direct contact with the skin. A layer of KY jelly was used as a medium between the probe and the skin. The probe was then pressed firmly onto the lesion. The freezing generally continued for the next 2-3 minutes or until a 1-3mm halo could be seen around the lesion. Immediately after treatment, participants were asked to fill in the VAS to measure the acute pain caused. The participants in this group were then reviewed 7 days following the initial interview for removal of the blister if required. Advice was given regarding re-dressing of the lesion for the following 2 weeks. The second interview was performed at time 1;3 weeks following initial treatment, where the lesion was re-measured with the graded scalpel handle and the FFI was filled in a second time.

Subjects in Group B received the following treatment: Cryotherapy using Nitrous Oxide (N_2O) as a cryogen. The N_2O in liquid form was sprayed from a pressurized canister by means of a portable cryotherapy device. This treatment involved a double freeze-thaw cycle while avoiding damage to healthy tissue. The duration of treatment differed according to the size of the lesion. Generally, the patient would give a visual sign that the healthy tissue had been reached as he would suddenly feel a change in the type of pain. Each shot lasted no longer than 30 seconds. A circulatory or zig-zag motion was used when performing the cryotherapy. The first freeze was followed by a second one 30 seconds after the first is stopped. Immediately after treatment, the patients were asked to fill in the VAS to measure acute pain caused by the treatment. Patients were then asked to attend the clinic 3 weeks following initial treatment (Time 1) where the size of the lesion was re-measured and recorded and the FFI was filled in again to measure quality of life in the week following initial treatment.

4. STATISTICAL ANALYSIS

All data collected was analyzed using PASW statistics software. The One way ANOVA, Paired sample T-Test and Independent sample T-test were used for analysis of data.

5. RESULTS

A total of 20 participants, 10 males and 10 females presenting for the first time with an untreated plantar wart were included in the study. The mean age for Group A was 40.2 and 34.9 for Group B. In this study, lesions were located as follows; 6 lesions on the 1st MPJ, 2 lesions on the hallux, 6 lesions on the heel and 6 lesions on the 5th MPJ.

For the purpose of this study, effectiveness of the treatments was measured in terms of reduction in size of lesions. Reduction in size was calculated from the values obtained at Time 0 and at Time 1. No significant difference was found in wart size (P=0.344) at the start of the study (Time 0) between groups. At time 1, two lesions were completely resolved following treatment, one lesion from each group. Following treatment with two different cryogens the mean reduction in size of wart in Group A was 1.85mm whilst in Group B mean reduction of wart size was 1.190mm. The One-Way Anova was used to calculate the difference in mean change in size of lesion between the two groups. No significant difference (P=0.387) was found in the mean reduction in size of plantar warts between the two treatment options.

The pain caused during treatment by the two treatment techniques was also measured in this study using the Visual Analogue Scale. The One-Way ANOVA was used to evaluate the difference in pain caused by the treatments. This study found no significant difference (P=0.855) in pain between the two cryotherapy techniques.

The paired sample T test was used to compare the mean Quality of Life score before and after each intervention in each group. No significant difference was found in FFI Pain Score (P=0.173), FFI Disability Score (P=0.136), and total change in QOL (P=0.188) from time 0 to time 1 following treatment using the CO2 Gun &Probe Cryotherapy, however a difference in mean scores were identified. No significant difference was found in FFI Pain score (P=0.881), FFI Disability score (P=0.351), FFI Activity Limitation (P=0.292) and Total change in QOL (P=0.297) from Time 0 to Time 1 following treatment with the N_2O portable pressurized spray technique. Although no significant difference was found, similar to Group A, a mean difference in scores was found in all scores of FFI from Time 0 to Time 1.

The One-Way ANOVA test was used to compare the mean Quality of Life (QOL) scores between two independent groups at the start of the study (Time 0). No significant difference was found between groups at Time 0 (P=0.874). The One-Way ANOVA was used to compare the FFI scores between both groups, at Time 1, in the week following the treatment. No statistical difference was found in Pain (P=0.237), Disability (P=0.161), Activity Limitation (P=0.242) and Total Change in QOL (P=0.172) between the two treatment techniques. Although results were found to be insignificant there was a difference in the mean scores for all FFI scores, implying that subjects in Group A experienced a higher degree of pain (52.19 vs. 37.706), disability (49.94 vs. 30.75), activity limitation (23.53 vs. 12.8) and total FFI scores (44.48 vs. 29.26) following treatment with CO_2 Gun & Probe cryotherapy technique when compared to the other cryogen.

6. DISCUSSION

The aim of this study was to compare differences in reduction in size, pain felt during application of treatment and change in quality of life before and after a single treatment for plantar warts using 2 different cryotherapy techniques namely the CO_2 Gun & Probe technique and the Portable N_2O pressurized spray technique. The key finding in this study was the fact that no significant difference in reduction in size, pain scores and FFI quality of life scores between the two groups. However this study has highlighted a mean difference in the FFI pain scores, disability scores, activity limitation and total scores between the two groups after a single treatment, implying that subjects in Group A experienced a higher degree of limitation of quality of life than patients treated in Group B. A key reason for this finding could be the sample size (n=20) used may be considered relatively small. Ideally larger cohorts would be recruited to increase statistical power of the study results. For this reason this study

could be considered as a pilot study and further research assessing the effectiveness of these two treatments is required in order to inform future practice especially in light that no such studies comparing two different cryogens for the treatment of plantar warts have been conducted.

Secondly, it has been suggested that a six month follow-up is a more realistic time point at which to assess the success of treatments of cutaneous warts than shorter time frames[5]. Participants in this study were not followed until full resolution. Participants in this study were assessed 3 weeks following first treatment. However we chose to assess the primary outcome in this study after one application with the different cryogen because the literature suggests that many plantar warts resolve spontaneously over time and if this had to be the case in our study population it would have been difficult to answer our clinical question and study aim.

Results of this study have concluded no significant difference between the two techniques when compared for effectiveness, pain caused during application of treatment and effect of quality of life before and after treatment. However mean scores have highlighted that although both treatments are effective in reducing the size of a plantar wart, Treatment A had a greater reduction in size of wart after one application than Treatment B. On the other hand Treatment A was reported to have caused more disablement to the patient following one application and a considerable reduction of quality of life was also noted.

No other studies have compared these two particular cryotherapy techniques before. Most studies[10,11,12,13] have compared a longer versus a shorter freeze, or a double versus a single freeze-thaw cycle. One study[12] used a cryoprobe, similar to the one used in treatment A of this study. Pooled data from all these studies concluded that the longer freeze was more effective than the shorter, and the double freeze more effective than the single freeze (52% versus 31%)[5]. In this study treatment A is more aggressive than treatment B due to the fact that it involves a longer freeze (3 mins vs approx 30 seconds). Therefore, the results from this study are congruent with the results from the studies above, implying that the longer the freeze the more effective the treatment.

Another important observation is that since N_20 pressurised spray cryotherapy device is portable, it could be considered for domiciliary care and for in-patient care, where it would be impractical to carry a heavy device like the CO_2 Gun & Probe. Health care professionals should therefore be aware of these two methods of cryotherapy, together with their advantages and disadvantages to be able to offer the best advice and treatment option to the patients who present at the clinic with a plantar wart.

7. CONCLUSION

Although this study has found no significant difference between two different techniques of cryotherapy, mean differences have indicated that the CO_2 Gun & Probe technique is more effective in reducing the size of the warts when compared to the N_2O Pressurized Spray Technique following one application; however the CO_2 Gun & Probe technique caused a larger impact on quality of life. Recommendations from this study suggest that careful consideration is required when selecting a treatment for plantar warts and furthermore patients should be advised on the likely outcomes of each treatment before any intervention. Further research is warranted to further investigate and explore the clinical efficacy of these two cryogens. Improved care could result in improved quality of life to people presenting with plantar warts and improved outcomes.

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